

DOCKET NO.: JANS-0027/JAB1498 US
 Application No.: 10/030,202
 Office Action Dated: October 20, 2004

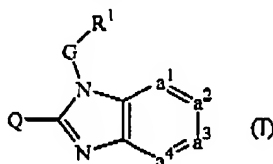
PATENT

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

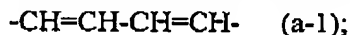
1. *(previously presented)* A method for treating respiratory syncytial viral infections, comprising the step of:

administering to a patient in need of such treatment, a composition comprising an effective amount of a compound of formula I:

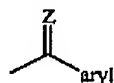


an addition salt or stereochemically isomeric form thereof,

wherein $-a^1=a^2-a^3=a^4-$ represents a bivalent radical of formula

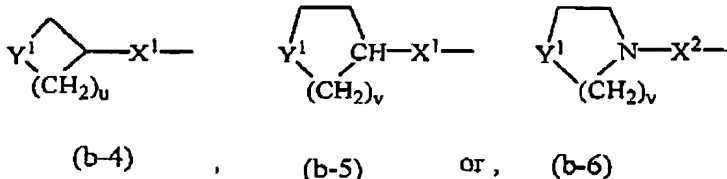


wherein each hydrogen atom in the radical (a-1) may optionally be replaced by halo, C_{1-6} alkyl, nitro, amino, hydroxy, C_{1-6} alkyloxy, polyhalo C_{1-6} alkyl, carboxyl, amino C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, hydroxy C_{1-6} alkyl, or a radical of formula



wherein Z is O, $\text{CH}-\text{C}(=\text{O})-\text{NR}^{5a}\text{R}^{5b}$, CH_2 , $\text{CH}-\text{C}_{1-6}\text{alkyl}$, N-OH or N-O- $\text{C}_{1-6}\text{alkyl}$;

Q is a radical of formula



DOCKET NO.: JANS-0027/JAB1498 US

Application No.: 10/030,202

Office Action Dated: October 20, 2004

PATENT

wherein

 Y^1 is a bivalent radical of formula $-NR^2-$ or $-CH(NR^2R^4)-$; X^1 is NR^4 , S, $S(=O)$, $S(=O)_2$, O, CH_2 , $C(=O)$, $C(=CH_2)$, $CH(OH)$, $CH(CH_3)$, $CH(OCH_3)$, $CH(SCH_3)$, $CH(NR^{5a}R^{5b})$, CH_2-NR^4 or NR^4-CH_2 ; X^2 is a direct bond, CH_2 , $C(=O)$, NR^4 , $C_{1-4}alkyl-NR^4$, $NR^4-C_{1-4}alkyl$;

u is 2 or 3;

v is 2; and

whereby each hydrogen atom in the carbocycles and the heterocycles defined in radicals (b-4), (b-5), and (b-6) may optionally be replaced by R^3 ; with the proviso that when R^3 is hydroxy or $C_{1-6}alkyloxy$, then R^3 can not replace a hydrogen atom in the α position relative to a nitrogen atom;

G is a direct bond or $C_{1-10}alkanediyl$;

R^1 is a monocyclic heterocycle selected from piperidiny, piperaziny, pyridyl, pyraziny, pyridaziny, pyrimidiny, pyrroly, furanyl, tetrahydrofuranyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, and isothiazolyl; and each heterocycle may optionally be substituted with 1 or where possible more substituents selected from halo, hydroxy, amino, cyano, carboxy, $C_{1-6}alkyl$, $C_{1-6}alkyloxy$, $C_{1-6}alkylthio$, $C_{1-6}alkyloxyC_{1-6}alkyl$, aryl, aryl $C_{1-6}alkyl$, aryl $C_{1-6}alkyloxy$, hydroxy $C_{1-6}alkyl$, mono-or di($C_{1-6}alkyl$)amino, mono-or di($C_{1-6}alkyl$)amino $C_{1-6}alkyl$, polyhalo $C_{1-6}alkyl$, $C_{1-6}alkylcarbonylamino$, $C_{1-6}alkyl-SO_2-NR^{5c}$, aryl- SO_2-NR^{5c} , $C_{1-6}alkyloxycarbonyl$, $-C(=O)-NR^{5c}R^{5d}$, $HO(-CH_2-CH_2-O)_n$, halo $(-CH_2-CH_2-O)_n$, $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$, aryl $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$ and mono-or di($C_{1-6}alkyl$)amino $(-CH_2-CH_2-O)_n$;

each n independently is 1, 2, 3 or 4;

R^2 is hydrogen, formyl, $C_{1-6}alkylcarbonyl$, Hetercarbonyl, pyrrolidiny, piperidiny, homopiperidiny, $C_{3-7}cycloalkyl$ substituted with $N(R^6)_2$, or $C_{1-10}alkyl$ substituted with $N(R^6)_2$ and optionally with a second, third or fourth substituent selected from amino, hydroxy, $C_{3-7}cycloalkyl$, $C_{2-5}alkanediyl$, piperidiny, mono-or

DOCKET NO.: JANS-0027/JAB1498 US

PATENT

Application No.: 10/030,202

Office Action Dated: October 20, 2004

di(C₁₋₆alkyl)amino,C₁₋₆alkyloxycarbonylamino, aryl and aryloxy;

R³ is hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, arylC₁₋₆alkyl or arylC₁₋₆alkyloxy;

R⁴ is hydrogen, C₁₋₆alkyl or arylC₁₋₆alkyl;R^{5a}, R^{5b}, R^{5c} and R^{5d} each independently are hydrogen or C₁₋₆alkyl; or

R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -(CH₂)_s- wherein s is 4 or 5;

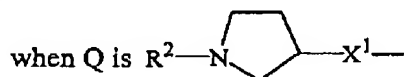
R⁶ is hydrogen, C₁₋₆alkyl, formyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl or C₁₋₆alkyloxycarbonyl;

aryl is phenyl or phenyl substituted with 1 or more-substituents selected from halo, hydroxy, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, polyhaloC₁₋₆alkyl, and C₁₋₆alkyloxy; and

Het is pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl;

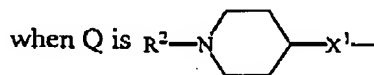
2. (cancelled)

- 3. (previously presented)** A method of treating a respiratory syncytial viral infection according to claim 10, wherein:



wherein X¹ is NR⁴, O, S, S(=O), S(=O)₂, CH₂, C(=O), C(=CH₂) or CH(CH₃), then R¹ is other than pyridyl, pyridyl substituted with C₁₋₆alkyl, pyrimidinyl, pyrazinyl, imidazolyl and imidazolyl substituted with C₁₋₆alkyl.

- 4. (previously presented)** A method of treating a respiratory syncytial viral infection according to claim 10, wherein:



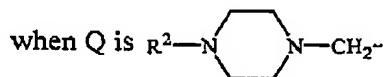
DOCKET NO.: JANS-0027/JAB1498 US
Application No.: 10/030,202
Office Action Dated: October 20, 2004

PATENT

wherein X^1 is NR^4 , O, S, $S(=O)$, $S(=O)_2$, CH_2 , $C(=O)$, $C(=CH_2)$ or $CH(CH_3)$, then R^1 is other than pyridyl, pyridyl substituted with C_{1-6} alkyl, pyridyl substituted with 1 or 2 C_{1-6} alkyloxy, pyrazinyl, pyrrolyl, pyrrolyl substituted with C_{1-6} alkyl, imidazolyl and imidazolyl substituted with C_{1-6} alkyl.

5. (cancelled)

6. (previously amended) A method of treating a respiratory syncytial viral infection according to claim 10, wherein:



then R^1 is other than pyridyl, pyrimidinyl, pyrazinyl, imidazolyl and imidazolyl substituted with C_{1-6} alkyl.

7. (cancelled)

8. (currently amended) A method of treating a respiratory syncytial viral infection comprising the step of administering a therapeutically effective amount of a compound, according to claim 10, wherein the compound is:

(±)-2-[[2-[[1-(2-amino-3-methylbutyl)-4-piperidiny]amino]-7-methyl-1H-benzimidazol-1-yl]methyl]-6-methyl-3-pyridinol tetrahydrochloride monohydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-1H-benzimidazol-1-yl]methyl]-3-pyridinol;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-6-chloro-1-[(1,4-dimethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazol-2-amine monohydrate;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-6-chloro-1-[(6-methyl-2-pyridiny]methyl]-1H-benzimidazol-2-amine;

N-[1-(2-aminoethyl)-4-piperidiny]-1-[[3-(2-ethoxyethoxy)-6-methyl-2-pyridiny]methyl]-1H-benzimidazol-2-amine tetrahydrochloride dihydrate;

DOCKET NO.: JANS-0027/JAB1498 US
Application No.: 10/030,202
Office Action Dated: October 20, 2004

PATENT

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-1-[(2-chloro-1,4-dimethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazol-2-amine;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-6-chloro-1-[(2-chloro-1,4-dimethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazol-2-amine;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-6-methyl-1-[(6-methyl-2-pyridiny)methyl]-1H-benzimidazol-2-amine;

(±)-N-[1-(2-aminopropyl)-4-piperidiny]-1-[(3,5,6-trimethylpyraziny)methyl]-1H-benzimidazol-2-amine tetrahydrochloride trihydrate;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-1-[(3,5,6-trimethylpyraziny)methyl]-1H-benzimidazol-2-amine;

N-[1-(2-aminoethyl)-4-piperidiny]-1-[[3-(2-chloroethoxy)-6-methyl-2-pyridiny)methyl]-1H-benzimidazol-2-amine trihydrochloride dihydrate;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-1-[(3-amino-2-pyridiny)methyl]-1H-benzimidazol-2-amine tetrahydrochloride trihydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride;

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-6-chloro-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride 2-propanolate (1:1);

(±)-2-[[2-[[1-(2-amino-3-methylbutyl)-4-piperidiny]amino]-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol;

(±)-2-[[2-[[1-(2-aminopropyl)-4-piperidiny]amino]-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride trihydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-7-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride dihydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-6-bromo-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride;

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride monohydrate;

DOCKET NO.: JANS-0027/JAB1498 US
Application No.: 10/030,202
Office Action Dated: October 20, 2004

PATENT

(±)-2-[[2-[[1-(2-amino-3-methylbutyl)-4-piperidiny]amino]-1H-benzimidazol-1-yl]methyl]-6-methyl-3-pyridinol;
(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-4-methyl-1-[(6-methyl-2-pyridiny)methyl]-1H-benzimidazol-2-amine; or
an addition salt or stereochemically isomeric form thereof.

9. (*currently amended*) A method of treating a respiratory syncytial viral infection comprising the step of administering a therapeutically effective amount of a compound, according to claim 10, wherein the compound is:

2-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-5-chloro-7-methyl-1H-benzimidazol-1-yl]methyl]-6-methyl-3-pyridinol tetrahydrochloride tetrahydrate;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(2,4-dimethyl-5-oxazolyl)methyl]-1H-benzimidazol-2-amine;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(2,5-dimethyl-4-oxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(5-methyl-3-isoxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-amine monohydrate;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;
N-[1-(2-aminoethyl)-4-piperidiny]-1-(4-thiazolylmethyl)-1H-benzimidazol-2-amine;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]-1H-benzimidazol-2-amine trihydrochloride;
5-[[2-[[1-(2-aminoethyl)-4-piperidiny]amino]-1H-benzimidazol-1-yl]methyl]-2-oxazolemethanol tetrahydrochloride dihydrate;
N-[1-(2-aminoethyl)-4-piperidiny]-1-[(3-methyl-5-isoxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;

DOCKET NO.: JANS-0027/JAB1498 US
 Application No.: 10/030,202
 Office Action Dated: October 20, 2004

PATENT

4-[[1-[[2-(dimethylamino)-4-thiazolyl]methyl]-1H-benzimidazol-2-yl]methyl]-1-piperidineethanamine tetrahydrochloride monohydrate 2-propanolate (1:1);

ethyl 5-[[2-[[1-[2-[[[(1,1-dimethylethoxy)carbonyl]amino]ethyl]-4-piperidinyl]amino]-1H-benzimidazol-1-yl]methyl]-2-methyl-4-oxazolecarboxylate;

4-[[1-[(2-methyl-4-thiazolyl)methyl]-1H-benzimidazol-2-yl]methyl]-1-piperidineethanamine;

N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-methyl-3-furanyl)methyl]-1H-benzimidazol-2-amine;

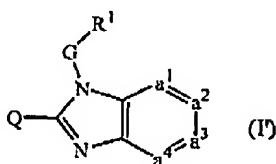
1,1-dimethylethyl 4-[[1-[[3-[2-(dimethylamino)ethoxy]]-6-methyl-2-pyridinyl]methyl]-1H-benzimidazol-2-yl]amino-1-piperidinecarboxylate;

ethyl 4-[[1-[(3-amino-2-pyridinyl)methyl]-1H-benzimidazol-2-yl]amino]-1-piperidinecarboxylate;

N-[1-(6-methyl-2-pyridinyl)-1H-benzimidazol-2-yl]-1-(3-pyridinylcarbonyl)-4-piperidinamine; or

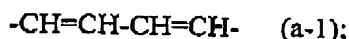
an addition salt or stereochemically isomeric form thereof.

10. *(previously presented)* A method of treating a respiratory syncytial viral infection, comprising the step of administering a therapeutically effective amount of said compound of formula (I'):



an addition salt, or stereochemically isomeric form thereof,

wherein $-a^1=a^2-a^3=a^4-$ represents a radical of formula

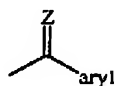


wherein each hydrogen atom in the radicals (a-1) may optionally be replaced by halo, C_{1-6} alkyl, nitro, amino, hydroxy, C_{1-6} alkyloxy, polyhalo C_{1-6} alkyl, carboxyl,

DOCKET NO.: JANS-0027/JAB1498 US
 Application No.: 10/030,202
 Office Action Dated: October 20, 2004

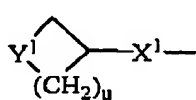
PATENT

aminoC₁₋₆alkyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, hydroxyC₁₋₆alkyl, or a radical of formula

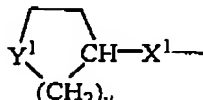


wherein Z is O, CH-C(=O)-NR^{5a}R^{5b}, CH₂, CH-C₁₋₆alkyl, N-OH or N-O-C₁₋₆alkyl;

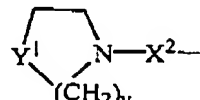
Q is a radical of formula



(b-4)



(b-5)



(b-6)

, (b-5) or, (b-6) ;

wherein

Y¹ is a bivalent radical of formula -NR²- or -CH(NR²R⁴)-;

X¹ is NR⁴, S, S(=O), S(=O)₂, O, CH₂, C(=O), C(=CH₂), CH(OH), CH(CH₃), CH(OCH₃), CH(SCH₃), CH(NR^{5a}R^{5b}), CH₂-NR⁴ or NR⁴-CH₂;

X² is a direct bond, CH₂, C(=O), NR⁴, C₁₋₄alkyl-NR⁴, NR⁴-C₁₋₄alkyl;

u is 2 or 3;

v is 2; and

whereby each hydrogen atom in the carbocycles and the heterocycles defined in radicals (b-4), (b-5), and (b-6) may optionally be replaced by R³; with the proviso that when R³ is hydroxy or C₁₋₆alkyloxy, then R³ can not replace a hydrogen atom in the α position relative to a nitrogen atom;

G is a direct bond or C₁₋₁₀alkanediyl;

R¹ is a monocyclic heterocycle selected from pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, pyrrolyl, imidazolyl and pyrazolyl; and each heterocycle may optionally be substituted with 1 or where possible more substituents selected from halo, hydroxy, amino, cyano, carboxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkyloxyC₁₋₆alkyl, aryl, arylC₁₋₆alkyl, arylC₁₋₆alkyloxy, hydroxyC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)amino, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, polyhaloC₁₋₆alkyl, C₁₋₆alkylcarbonylamino,

DOCKET NO.: JANS-0027/JAB1498 US
 Application No.: 10/030,202
 Office Action Dated: October 20, 2004

PATENT

C_{1-6} alkyl-SO₂-NR^{5c}-, aryl-SO₂-NR^{5c}-, C_{1-6} alkyloxycarbonyl, -C(=O)-NR^{5c}R^{5d},
 HO(-CH₂-CH₂-O)_n-, halo(-CH₂-CH₂-O)_n-, C_{1-6} alkyloxy(-CH₂-CH₂-O)_n-,
 aryl C_{1-6} alkyloxy(-CH₂-CH₂-O)_n- and mono-or di(C_{1-6} alkyl)amino
 (-CH₂-CH₂-O)_n-;

each n independently is 1, 2, 3 or 4;

R² is hydrogen, formyl, pyrrolidinyl, piperidinyl, homopiperidinyl,
 C_{3-7} cycloalkyl substituted with N(R⁶)₂, or C_{1-10} alkyl substituted with N(R⁶)₂ and
 optionally with a second, third or fourth substituent selected from amino, hydroxy, C_{3-7}
 cycloalkyl, C_{2-5} alkanediyl, piperidinyl, mono-or di(C_{1-6} alkyl)amino,
 C_{1-6} alkyloxycarbonylamino, aryl and aryloxy;

R³ is hydrogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkyloxy, aryl C_{1-6} alkyl or
 aryl C_{1-6} alkyloxy;

R⁴ is hydrogen, C_{1-6} alkyl or aryl C_{1-6} alkyl;

R^{5a}, R^{5b}, R^{5c} and R^{5d} each independently are hydrogen or C_{1-6} alkyl; or

R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -
 (CH₂)_s- wherein s is 4 or 5;

R⁶ is hydrogen, C_{1-4} alkyl, formyl, hydroxy C_{1-6} alkyl, C_{1-6} alkylcarbonyl or
 C_{1-6} alkyloxycarbonyl;

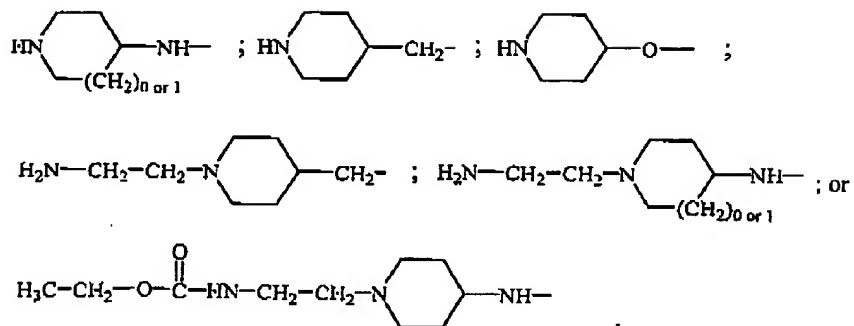
aryl is phenyl or phenyl substituted with 1 or more substituents selected from
 halo, hydroxy, C_{1-6} alkyl, hydroxy C_{1-6} alkyl, polyhalo C_{1-6} alkyl, and C_{1-6} alkyloxy;

provided:

that when G is methylene, and R¹ is 2-pyridyl, 3-pyridyl, 6-methyl-2-
 pyridyl, 2-pyrazinyl or 5-methyl-imidazol-4-yl, then Q is other than

DOCKET NO.: JANS-0027/JAB1498 US
Application No.: 10/030,202
Office Action Dated: October 20, 2004

PATENT

Claims 11 to 22 (*cancelled*)